

I. Rejection Under 35 U.S.C. §103

Claims 1-144 [sic, claims 1-52 and 54-144] are rejected under 35 U.S.C. §103(a) over WO '598 or WO '797. Because the disclosures of these references are similar, at least with respect to their applicability to the present claims, the references will be addressed together. Applicants respectfully traverse these rejections.

A. Independent Claim 1

Claim 1 is directed to a method of applying at least one agent selected from the group consisting of bioactive materials, flavorants, polymerization initiators, and polymerization rate modifiers to an applicator tip for an adhesive applicator, comprising: dissolving or dispersing said agent in a low boiling point solvent to form a solution; applying said solution to said applicator tip; and drying said applicator tip; wherein the low boiling point solvent comprises methanol. Such a method is nowhere taught or suggested in the cited references.

1. The References Do Not Teach or Suggest Using Methanol

An aspect of the claimed invention is that while the various materials may be applied to the applicator tip in a number of different ways or in a number of solutions, the use of a solution comprising methanol provides a distinct advantage. In particular, as described in the specification, the present inventors discovered that the use of methanol, alone or as a component of a mixture of low boiling point solvents, provides an unexpectedly superior distribution profile of the material on, and within, the applicator tip. Specification at page 6, lines 2-6. In particular, the superior distribution profile allows a reduction in polymerization time of the dispensed monomeric adhesive while avoiding tissue damage due to the highly exothermic polymerization reaction. Specification at page 6, lines 6-9.

The cited references fail to teach or suggest applying the specified agents to an applicator tip using a solvent comprising methanol. At most, WO '598 discloses that "the applicator tip material may be porous, absorbent or adsorbent in nature to enhance and

facilitate loading of the initiator on or within the applicator tip." Page 18, lines 34-36. The reference then discloses that the initiators "may be applied to a surface portion or to the entire surface of the applicator tip, including the interior and the exterior of the tip." Page 19, lines 15-18. Finally, WO '598 discloses that a liquid medium used to apply the initiator "may include non-aqueous solvents, such as ether, acetone, ethanol, pentane or mixtures thereof, or may include aqueous solutions. Preferably the liquid medium is a low boiling point solvent." Page 20, line 37 to page 21, line 4.

WO '797 includes substantially similar disclosures. See, for example, page 15, lines 15-18; page 15, line 35 to page 16, line 4; and page 17, lines 24-28.

Thus, while WO '598 and WO '797 disclose that a low boiling point solvent can be used, and disclose various suitable solvents, the references do not teach or suggest the use of a low boiling point solvent that comprises methanol, as claimed. Nor does either reference teach or suggest that methanol could or should be used in place of or in addition to any of the specified solvents. Accordingly, the references would not have rendered obvious to one of ordinary skill in the art the invention of independent claim 1, and the claims dependent therefrom.

2. The Claimed Invention Provides Unexpected Results

Furthermore, the selection of methanol as a solvent for applying the agent provides unexpected results that are not taught or suggested by the cited references. Such unexpected results overcome any prima facie case of obviousness that may be considered to have been established by the Office Action.

As mentioned above, the use of methanol provides an unexpectedly superior distribution profile of the material on, and within, the applicator tip. This different distribution profile, in turn, allows a reduction in polymerization time of the dispensed

monomeric adhesive while avoiding tissue damage due to the highly exothermic polymerization reaction. Specification at page 6, lines 2-9.

At most, the cited references teach that a variety of solvents can be used, but that comparable results would be achieved regardless of the selection of solvent. That is, nowhere does either cited reference teach or suggest that different results would be obtained if one solvent were selected over another solvent. In contrast, the present specification provides express exemplary evidence that different and unexpected results are obtained based on the solvent selection.

At page 9, the present specification describes comparative testing of applicator tips made according to the claimed invention versus applicator tips made according to U.S. Patent No. 5,928,611, which corresponds to WO '797 and is comparable to WO '598. The specification describes that initiator-loaded applicator tips were produced by applying a polymerization initiator or a polymerization rate modifier (benzalkonium chloride) to the tip by pumping a liquid medium comprising the initiator or rate modifier through a syringe and onto the distal end of the tip. Separate initiator-loaded tips were prepared by using a solution of the initiator or rate modifier dissolved in 110 μ L of various solvents. Page 9, line 28 to page 10, line 9. The tips were prepared using the solvents acetone (disclosed in the Examples of WO '797) and methanol (according to the claimed invention).

In the case where acetone was used, the specification describes that different results were obtained when the applicator tips are used to apply a polymerizable cyanoacrylate adhesive material. For example, the specification describes that it can be shown using thermal analysis techniques such as differential scanning calorimetry, that monomer compositions applied through the different applicator tips generate different amounts of heat. If the peak temperature of heat generated is too high, then the heat can be damaging to tissues. Page 9, lines 14-16. For example, as shown in Figure 5, a composition comprising 2-octyl

cyanoacrylate dispensed through an applicator tip having an initiator (benzalkonium chloride) applied with acetone generates heat having a peak temperature of about 80°C. Page 9, lines 16-20. However, the same composition dispensed through a tip having the same initiator applied using methanol according to the claimed invention shows a much lower peak temperature of approximately 40°C. Page 9, lines 20-22.

Furthermore, as shown in Figure 6 of the specification, the setting time, or the amount of time required for polymerization, of a 2-octyl cyanoacrylate composition is slightly longer when the cyanoacrylate composition is dispensed through a tip having a benzalkonium chloride initiator disposed thereon using methanol as compared to using acetone. See specification at Fig. 6 and page 9, lines 23-27.

These results, presented in the present specification, demonstrate that the applicator tips of WO '797 (and WO '598) are different from the applicator tips of the claimed invention, and that the applicator tips of the claimed invention provide significant and unexpected benefits not disclosed in the cited references.

3. Methanol as a Homolog of Ethanol Does Not Establish Obviousness

The Office Action argues that the claimed invention would further have been obvious over the cited references because the references disclose the use of ethanol, and the claimed use of methanol is merely a homolog of the disclosed ethanol. However, this fact alone does not establish obviousness of the claimed invention.

Although the instantly claimed methanol may be a homolog of the disclosed ethanol, the asserted homology alone would not have rendered obvious the claimed invention. In particular, the law of homology is based on the assumption that similar compounds will provide similar results. However, as described above, the claimed invention provides unexpected results over the disclosure of the cited references. The present specification

explicitly discloses that in fact the claimed invention provides significantly different results from the cited references.

Although the above discussion of unexpected results is with respect to a comparison of methanol and acetone, the disclosure of the cited references at most teaches that the disclosed compounds, including ethanol and acetone, would provide the same results. Thus, the present comparison of results using methanol to results using the disclosed acetone can also be treated as a comparison of the claimed invention to results using the disclosed ethanol. Any argument to the contrary would mean that the various disclosed solvents in the cited references provide different and/or unpredictable results from each other. In that case, it would likewise be improper to assert that the claimed methanol would provide expected comparable results to any of the disclosed solvents.

4. Conclusion

Accordingly, for at least these reasons, the references cannot have rendered obvious to one of ordinary skill in the art the invention of independent claim 1, and the claims dependent therefrom. Reconsideration and withdrawal of the rejection with respect to these claims are respectfully requested.

B. Independent Claims 26 and 76

Amended independent claim 26 is directed to a method of making an applicator for adhesives, comprising: preparing a conduit for a fluid polymerizable adhesive composition operably connected to an applicator tip so that fluid flowing through said conduit also flows through said applicator tip, wherein an agent is included on or in said applicator tip, wherein said agent is selected from the group consisting of (a) a bioactive material that is not also a polymerization initiator or a polymerization rate modifier, (b) a bioactive material that is also a polymerization initiator or a polymerization rate modifier, (c) a polymerization initiator that is not also a bioactive material, (d) a polymerization rate modifier that is not also a bioactive

material, and (e) a flavorant, and wherein the agent is dissolved or dispersed in a solvent comprising methanol to form a solution, and said solution is applied to said applicator tip, at least when the agent is (b), (c) or (d).

Similarly, amended independent claim 76 is directed to an applicator for a polymerizable adhesive, comprising: an applicator tip attached to an applicator body, and at least one agent on or in said applicator tip, wherein said agent is selected from the group consisting of (a) a bioactive material that is not also a polymerization initiator or a polymerization rate modifier, (b) a bioactive material that is also a polymerization initiator or a polymerization rate modifier, (c) a polymerization initiator that is not also a bioactive material, (d) a polymerization rate modifier that is not also a bioactive material, and (e) a flavorant, and wherein the agent is dissolved or dispersed in a solvent comprising methanol to form a solution, and said solution is applied to said applicator tip, at least when the agent is (b), (c) or (d).

Accordingly, claims 26 and 76 require that methanol be used in a solution to apply the agent to the applicator tip, except where the agent is either (i) a bioactive material that is not also a polymerization initiator or a polymerization rate modifier, or (ii) a flavorant. Such a method and applicator are not taught or suggested in the cited references.

As described above, the cited references fail to teach or suggest applying an agent to the applicator tip in a solution, where the solution includes a low boiling point solvent that comprises methanol, as claimed. The cited references further fail to teach or suggest the unexpected results that are provided by the use of methanol as a solvent. Thus, with respect to this embodiment of the claims, the rejection is overcome and should be withdrawn.

Moreover, with respect to the embodiments of the claims where methanol is not required, the references also fail to teach or suggest either applying a flavorant to the

applicator tip, or applying a bioactive but non-initiator or -rate modifier to the applicator tip, as claimed.

Markush
As described in the Office Action, both WO '598 and WO '797 are directed to methods and applicator tips where a polymerization initiator or rate modifier is applied to an applicator tip. However, the references do not teach or suggest that other materials could or should be applied to the applicator tip. Thus, neither reference teaches or suggests that a flavorant could or should be applied to the applicator tip. Likewise, neither reference teaches or suggests that a material, which is not a polymerization initiator or rate modifier, could or should be applied to the applicator tip.

In order to have rendered obvious the claimed invention, the reason, suggestion or motivation for combining the references or for modifying their disclosures "can not come from the applicant's invention itself." In re Oetiker, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). That is, the motivation for combining or modifying the references can not be a product of hindsight reconstruction of the claimed invention based on applicant's own disclosure.

Such a hindsight reconstruction has clearly been made in the present Office Action. The Office Action asserts that the claimed invention would have been obvious based on a hindsight evaluation of the claimed invention and the cited references. Because neither reference teaches or suggests that a flavorant or that a bioactive but non-polymerization initiator or rate modifier could or should be applied to an applicator tip, the only motivation for doing so comes from Applicants' present invention. However, deriving the claimed invention in this manner is improper because the references, viewed by themselves and not in retrospect, must suggest the combination asserted by the Office Action. In re Shaffer, 229 F.2d 476, 108 USPQ 326 (C.C.P.A. 1956); In re Stoll, 523 F.2d 1392, 187 USPQ 481 (C.C.P.A. 1975). Here the references do not provide any motivation for modifying the references so as to arrive at the claimed invention; the only motivation for modifying the cited references in the manner asserted

in the Office Action derives from the disclosure of the present application, which is clearly improper.

Accordingly, for at least these reasons, the references cannot have rendered obvious to one of ordinary skill in the art the invention of independent claims 26 and 76, and the claims dependent therefrom. Reconsideration and withdrawal of the rejection with respect to these claims are respectfully requested.

C. Independent Claim 50

Independent claim 50 is directed to a method of applying at least one agent selected from the group consisting of bioactive materials, flavorants, polymerization initiators, and polymerization rate modifiers to an applicator tip for an adhesive applicator, comprising: dissolving, dispersing or suspending said agent in a liquid medium to form a suspension or solution; combining said suspension or solution and said applicator tip in a vessel; sealing said vessel; applying one of a vacuum or pressure to said vessel to degas air trapped in said applicator tip; releasing said vacuum or pressure; and optionally drying said applicator tip. Such a method is nowhere taught or suggested by the cited references.

The method of claim 50 is directed to an improved method for applying the respective agents to an applicator tip. According to the claimed method, application of the vacuum or pressure results in air that is trapped in the applicator tips being degassed, or forced out of the applicator tips, and being replaced by the solution or suspension including the desired agent. This replacement of air by the solution or suspension thereby loads the material onto or into the applicator tips. Specification at page 11, lines 18-24. The claimed method thus results in an improved loading of the agent into the applicator tip.

In contrast to the claimed invention, WO '598 and WO '797 merely disclose that "the initiator may be applied to the applicator tip by spraying, dipping, or brushing the applicator tip with a liquid medium containing the initiator." See WO '598 at page 20, lines 34-37; WO

'797 at page 17, lines 21-24. Nowhere does either reference teach or suggest that the initiator, or other instantly claimed agent, could or should be applied to the applicator tip by a method specifically utilizing vacuum or pressure to force the agent into the applicator tip.

As described above, in order for a reference to have rendered obvious the claimed invention, the claimed invention must have been obvious to one of ordinary skill in the art over the cited reference. The motivation to modify the cited references cannot come from Applicants' own disclosure. However, nowhere does either reference teach the use of vacuum or pressure to apply an agent to an applicator tip. Nor does either reference even suggest that such vacuum or pressure could even be used.

The Office Action entirely fails to specify why one of ordinary skill in the art would have been motivated to somehow modify the processes disclosed in the cited references to arrive at the claimed invention. The Office Action does not describe why one of ordinary skill in the art would have substituted the claimed use of vacuum or pressure for the disclosed use of spraying, dipping, or brushing. In the absence of any such teachings, the cited references cannot have rendered obvious the claimed invention.

The Office Action attempts to overcome this deficiency of the references by arguing that the references "disclose heating the applicator tip in a vacuum oven." However, that disclosure of the references is taken out of context, and does not teach or suggest the claimed invention.

As pointed out in the Office Action, the references make reference to the use of a vacuum oven. However, the vacuum oven is not used to apply the material to the applicator tip, as claimed. Rather, the references merely disclose that "Subsequent to application of the initiator on or in the applicator tip, the applicator tip may be dried or heated to evaporate or volatilize the liquid medium or to evenly distribute or impregnate initiator in the applicator tip." WO '797 at page 18, lines 7-15 (emphasis added).

Accordingly, for at least these reasons, the references cannot have rendered obvious to one of ordinary skill in the art the invention of independent claim 50 and the claims dependent therefrom. Reconsideration and withdrawal of the rejection with respect to these claims are respectfully requested.

D. Independent Claim 52

Independent claim 52 is directed to a method of making an applicator tip for an adhesive applicator, comprising: loading at least one active member selected from the group consisting of bioactive materials, flavorants, polymerization initiators and polymerization rate modifiers on an applicator tip prior to or during manufacturing of a structural material or shape of the applicator tip. Such a method is not taught or suggested in the cited references.

Claim 52 is directed to a method of making an applicator tip for an adhesive applicator, comprising: loading at least one active member selected from the group consisting of bioactive materials, flavorants, polymerization initiators and polymerization rate modifiers on an applicator tip prior to or during manufacturing of a structural material or shape of the applicator tip, wherein the applicator tip is formed of a reticulated material. The references fail to teach or suggest at least the limitation that the applicator tip is made of a reticulated material.

At most, the references disclose that a porous material, which can be absorbent or adsorbent, is used as an applicator tip. However, the references contain no disclosure regarding the specifics of the applicator tip with respect to the type of material that could or should be used. The references fail to teach or suggest that the applicator tip should in particular be made of a reticulated material. Thus, the references fail to teach or suggest each and every limitation of the claimed invention

In response, the Office Action cites a dictionary definition for the assertion that "reticulated" means "constructed so as to form a network." However, regardless of this

definition, the fact remains that neither reference teaches or suggests the use of a reticulated material for the applicator tip. The references' disclosure of the use of a porous material would not have rendered obvious the use of every possible type of porous material, or the use of a reticulated material in particular.

As described repeatedly above, the references must have rendered obvious the claimed invention, including each and every limitation of the claims, to one of ordinary skill in the art. Even taking the Office Action's definition of "reticulated," which Applicants do not necessarily accept as being the accepted definition in the art, that definition is nowhere specifically taught or suggested by the cited references. Thus the claimed invention can not have been obvious over the references.

Accordingly, for at least these reasons, the references cannot have rendered obvious to one of ordinary skill in the art the invention of independent claim 52 and the claims dependent therefrom. Reconsideration and withdrawal of the rejection with respect to these claims are respectfully requested.

E. Independent Claim 123

Independent claim 123 is directed to an applicator for a polymerizable adhesive comprising: a conduit for a fluid polymerizable adhesive material; and an applicator tip operably connected to said conduit so that fluid flowing through said conduit also flows through said applicator tip; wherein said applicator tip has a gradient of a polymerization initiator or polymerization rate modifier disposed therein. Such an applicator is not taught or suggested by the cited references.

1. The References Do Not Teach or Suggest a Concentration Gradient

The claimed invention is distinct from the applicator tip disclosed in WO '598 or WO '797. In contrast to the claimed applicator tip that has a concentration gradient of a polymerization initiator or polymerization rate modifier disposed therein, the cited references

merely disclose that an initiator can be applied to the surface or internal portions of an applicator tip. The references nowhere teach or suggest that the initiator can be applied to the bulk material of an applicator tip, such that a concentration gradient of the initiator is provided.

At most, the references disclose that the initiator can be applied in solution with a low boiling point solvent. WO '598 at page 20, line 37 to page 21, line 4, and WO '797 at page 17, lines 24-28. However, an important feature of the claimed invention is that the initiator can be applied in an anisotropic distribution or concentration gradient, rather than at a constant concentration, throughout the applicator tip. As such, a greater concentration of the initiator can be provided at either the front or back end of the applicator tip, to provide for more preferable mixing with and initiation of the monomer material. For example, the present specification teaches that a concentration gradient can be provided, that increases or decreases from the beginning of the applicator tip to the end of the applicator tip. Page 6, lines 25-31; page 9, line 28 to page 10, line 9.

Thus, the present claimed invention specifically provides for a concentration gradient of the initiator, whereas no such concentration gradient is taught or suggested by WO '598 or WO '797. While the cited references teach that the initiator can be applied either on the applicator tip surface or inside the applicator tip matrix, the references do not teach or suggest that the initiator can be applied inside the applicator tip matrix in a concentration gradient profile to provide improved mixing properties. In the absence of such a teaching, one of ordinary skill in the art would not have been motivated to modify the teachings of WO '598 or WO '797 to practice the claimed invention.

2. The Office Action Misunderstands the Claim Limitation

In response, the Office Action admits that the references do not disclose the concentration gradient. However, the Office Action argues that "it would have been obvious

to one skilled in the art at the time of the invention to utilize a concentration gradient to allow the agent to flow from the conduit to the applicator tip." However, this argument has nothing to do with the instant claim limitation, and appears both incorrect and irrelevant.

As claimed, the concentration gradient is a concentration gradient present in the applicator tip itself, and is a concentration gradient of the polymerization initiator or polymerization rate modifier, which is disposed in the applicator tip itself. That is, the polymerization initiator or polymerization rate modifier is disposed in the applicator tip in a fashion that forms a concentration gradient.

With respect to the Office Action's assertions, the agent does not "flow from the conduit to the applicator tip." Rather, the polymerization initiator or polymerization rate modifier is disposed in the applicator tip itself, and it is the fluid, i.e., adhesive, that flows through the conduit then through the applicator tip.

Furthermore, even if the Office Action's assertion was true, which it is not, the Office Action provides no explanation of why a concentration gradient would have any effect on the flow of the agent. Moreover, the Office Action fails to describe why the claimed concentration gradient would have been obvious over the cited references, where a concentration gradient is not formed.

The Office Action cannot merely pick a limitation from the present claims, and make a blanket assertion that the limitation would have been obvious. The Office Action must establish why the limitation would have been obvious over the cited references. The Office Action has failed to satisfy this burden.

3. Conclusion

Accordingly, for at least these reasons, the references cannot have rendered obvious to one of ordinary skill in the art the invention of independent claim 123 and the claims

dependent therefrom. Reconsideration and withdrawal of the rejection with respect to these claims are respectfully requested.

F. Independent Claim 135

Independent claim 135 is directed to an applicator for applying a polymerizable monomeric adhesive composition, comprising: an applicator body, and an applicator tip attached to the applicator body, wherein said applicator body is free of a polymerizable adhesive reservoir, and wherein at least one agent selected from the group consisting of bioactive materials, flavorants, polymerization initiators, and polymerization rate modifiers is present on or in said applicator tip. Such an applicator is not taught or suggested in the cited references.

WO '598 and WO '797 fail to teach or suggest that the applicator is "free of a polymerizable adhesive reservoir" as claimed. Both references disclose applicator containers that contain an amount of adhesive material, that is applied to a desired surface by expressing the material through the applicator tip. See, for example, WO '598 at page 17, lines 25-37 and WO '797 at Figures. WO '598 discloses that the applicator can be, for example, a crushable swab applicator, a syringe, a vial, an adhesive gun, a pipette, and an eyedropper. See WO '598 at page 17, line 29; and page 18, line 18. WO '797 has a similar disclosure. See WO '797 at page 14, lines 34-38.

However, neither reference teaches or suggests an applicator tip attached to an applicator body that is free of a polymerizable adhesive reservoir, and where at least one agent selected from the group consisting of bioactive materials, flavorants, polymerization initiators, and polymerization rate modifiers is present on or in the applicator tip, as claimed. Nowhere does either reference appear to teach or suggest that the applicator should be provided such that it is free of a polymerizable adhesive reservoir.

In fact, providing the applicators of WO '598 and WO '797 to be free of a polymerizable adhesive reservoir, would appear to be directly contradictory to the disclosures of the references. The references' focus upon applicators having an adhesive reservoir would not have led one of ordinary skill in the art to have removed the reservoir from the applicator. Nowhere does either reference teach or suggest how that applicator could be used in such an instance if the reservoir was removed.

In response, the Office Action merely argues that the references disclose "that the applicator body is a swab." However, the Office Action neither cites to a particular disclosure of the references, nor explains how such asserted disclosure would have rendered obvious the claimed invention. For example, the references' disclosure that the applicator can be a "crushable swab" does not correspond to, and would not have rendered obvious, the claimed invention that is specifically free of a polymerizable adhesive reservoir.

Accordingly, for at least these reasons, the references cannot have rendered obvious to one of ordinary skill in the art the invention of independent claim 135 and the claims dependent therefrom. Reconsideration and withdrawal of the rejection with respect to these claims are respectfully requested.

G. Conclusion

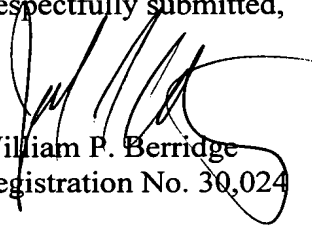
For at least these reasons, WO '598 and WO '797 would not have rendered obvious the claimed invention to one of ordinary skill in the art. Reconsideration and withdrawal of the rejections are respectfully requested.

II. Conclusion

In view of the foregoing remarks, Applicants submit that this application is in condition for allowance. Favorable reconsideration and prompt allowance of the application are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below.

Respectfully submitted,


William P. Berridge
Registration No. 30,024

Joel S. Armstrong
Registration No. 36,430

WPB:JSA

Date: December 17, 2001

OLIFF & BERRIDGE, PLC
P.O. Box 19928
Alexandria, Virginia 22320
Telephone: (703) 836-6400

<p>DEPOSIT ACCOUNT USE AUTHORIZATION Please grant any extension necessary for entry; Charge any fee due to our Deposit Account No. 15-0461</p>
--